III. BENEFITS OF THE FINAL RULE

This chapter discusses the ways in which the regulation of microorganisms under TSCA will result in the realization of certain societal benefits. Specifically, EPA regulation of such products, as set forth in the rule, is expected to reduce risks to health and the environment while concurrently resulting in greater regulatory efficiency and possibly improving the pace of product commercialization. This is accomplished by reducing regulatory burdens associated with microorganisms that pose the least likelihood of exhibiting new behaviors or new phenotypic traits. Thus, the risk reduction potential of EPA's rules under TSCA will be concentrated on those microorganisms posing the greatest uncertainty concerning risk to human health or the environment.

Unfortunately, risks to human health and the environment associated with microorganisms cannot be quantified accurately with information currently available or, in some cases, even identified with confidence. This chapter, therefore, provides a qualitative and necessarily incomplete assessment of possible risk reduction due to microbial regulation under TSCA. The chapter is organized as follows:

- Section A provides an overview of possible adverse impacts of genetically modified, novel microorganisms;

- Section B presents an assessment of the risk reduction potential of the rule; and

- Section C presents a qualitative assessment of the benefits associated with the rule.

A. Overview of Risks of Novel Microorganisms

There has been much discussion of whether possible hazards are associated with the use of certain genetically modified organisms, including reports such as those from the Ecological Society of America (Tiedje 1989),

the National Academy of Sciences (NAS 1987 and National Research Council 1989), and the Office of Technology Assessment (OTA 1988).

A number of important features distinguish microorganisms from traditional chemicals and under some circumstances could contribute to uncertainty concerning their risk. These features include the potential for microorganisms to spread and multiply in the environment (sometimes from very small initial populations), the ability to evolve, the ability to exchange genetic information with other microorganisms, the ability to continually produce proteins that may be ecologically disruptive or toxic to plants or animals, the ability to interact with other organisms through competition for resources within an ecosystem, and the possible displacement of members of natural microbial communities.

Possible adverse impacts could include health effects on humans, animals, and plants; increased costs or decreased productivity in farming and other areas of the economy; and ecological impacts whose long run health or economic effects may not be immediately apparent. At present, there is uncertainty as to the likelihood of these adverse impacts and their relationship to the use of microorganisms reportable under the rule.

Potential risks of environmental use of microorganisms must be assessed through consideration of characteristics of the microorganisms, the environment into which they will be released, and the environments into which they are capable of spreading (OTA 1988, NAS 1987, NAS 1989, Tiedje 1989). The Ecological Society of America identified examples of some potential outcomes associated with the development of engineered organisms that are to be avoided (Tiedje 1989):

- The creation of new pests.
- Enhancement of the effects of existing pests through transfer of an introduced trait.

- Disruptive effects on biotic communities. For example, the introduction into certain agricultural fields of the highly competitive non-indigenous nitrogen-fixing bacterium, Bradyrhizobium serogroup 123, has made it difficult to introduce potentially more effective rhizobia in those fields.

- Adverse effects on ecosystem processes. For example, the increased expression of microbial ligninase or constitutive denitrification could alter nutrient cycling adversely.

- Incomplete degradation of hazardous chemicals leading to the production of even more toxic by-products. For example, the microbial degradation of trichloroethylene (TCE) and tetrachloroethylene (or perchloroethylene, PCE) produces the more toxic substance vinyl chloride.

- Squandering of valuable biological resources. For example, genes for toxins produced by strains of certain bacteria have been inserted into crop plants and trees, conferring resistance against some pests. However, the genetically engineered crops as well as the unaltered bacteria could be rendered ineffective by creating conditions that accelerate the evolution of pest resistance.

B. Risk Reduction from Microbial Regulation

The principal benefits of the rule accrue through the avoidance of costs that would be borne by society in the event that regulatory oversight as outlined in the rule is not instituted. Such costs would result from damage to human health and the environment. To avoid these costs, the provisions of the rule have been designed to reduce risks associated with the introduction of new microorganisms into the environment.

This section first presents a qualitative assessment of the risk reduction potential of the requirements of the rule and then summarizes the points in the product development and regulatory process at which actions taken in response to regulatory oversight may be triggered, thereby directly reducing risk.

1. Risk Reduction Potential of Informational Requirements

In order for EPA to make a determination as to whether a particular microorganism may present risks to society, certain data regarding the identity, genetic makeup, and behavior of the new microorganisms are

necessary. Thus, the rule contains provisions asking for the submission of data that describe:

- the recipient microorganism and the new microorganism;
- the genetic construction of the new microorganism; and
- phenotypic and ecological characteristics associated with the new microorganism.

In addition to the microbiological data necessary to identify the microorganisms involved in a project, EPA requires researchers/manufacturers to submit information describing the activity for which the microorganism was developed. In the case of environmental releases for research and development, informational requirements include:

- a detailed description of the research and development activity, including rationale, number of cells and application method, and characteristics of the test site; and
- information on monitoring, confinement, mitigation, and emergency termination procedures.

In the case of releases associated with the general commercial use of a new microorganism subject to reporting under the rule, informational requirements include:

- total production volume;
- a description of the intended categories of use; and
- information describing worker exposure and environmental releases.

The availability of these data will ensure that EPA is well informed on the potential fate of microorganisms and able to quickly evaluate the consequences of an environmental release and identify potential untoward effects that might result. The Agency and/or the submitter may then act to ensure that the use of the microorganisms presents no unreasonable risks.

It should be noted that EPA recognizes that the incremental benefits realized in connection with reporting via the two main reporting vehicles

established in the rule (the MCAN and the TERA) will not be of similar magnitude in all cases. For example, exemptions from full reporting will be granted for contained structure uses under certain conditions. These exemptions reduce costs where incremental benefits of full reporting were estimated to be somewhat lower than in unfamiliar cases or cases where control mechanisms are judged to be adequate to ensure that unreasonable risks have been mitigated. Also, since these exemptions generally apply to widely used microorganisms, the overall reporting burden will be minimized under the rule. Thus, the rule has been designed to allow flexibility.

Finally, EPA requires the submission of all reasonably ascertainable data pertaining to subject microorganisms' effects on health and the environment. These data are of obvious value to the Agency in its efforts to prevent unreasonable risk. Also, since the microorganisms in question are "new", not all data on health and environmental effects would be expected to exist in the public domain.

It is not possible to estimate the proportion of overall benefit provided by each of the categories of information described above. Each, however, is essential if the rule is to maximize overall risk reduction benefits.

2. Risk Reduction Associated with Documentation and Recordkeeping Requirements

In addition to reporting requirements, the rule contains provisions requiring that certain records be maintained. All persons filing notices and applications in connection with the general commercial use of a microorganism will be required to maintain records of all data included in the submission. Those persons commencing work will be required to maintain records that document the date of commencement and, if manufacturing,

importing, or processing, the production volumes generated or used during three years of operations.

Records would also need to be maintained in support of certain exemptions (such as the exemption for "small quantities" of microorganisms intended for R&D use in a contained structure).

These requirements contribute to overall risk reduction by requiring researchers to address risk considerations in the planning and execution of research, by ensuring that a responsible official also addresses these considerations, and by enabling EPA to perform more meaningful inspections. In many cases, approvals for commencement of work may be granted without Agency imposed restrictions being placed on the activity in question. However, in other cases, approvals or exemptions may be granted based on specific information that the submitter has provided to Agency reviewers. In cases where a determination was made that risk would be maintained at reasonable levels based on certain containment and/or control mechanisms described by the submitter, on-site verification by EPA field staff that precautions were indeed being properly implemented would be possible. Similarly, on-site verification in association with work being performed by submitters operating under a consent order or TERA agreement is only possible if a record of the submission and agreement or order is available to the inspector.

3. Risk Reduction Potential of Consent Orders and TERA Agreements

Once EPA has ascertained the potential risk posed by a particular microbiological product, action may be taken under TSCA to prevent unreasonable risk. If, prior to granting approval for the general commercial use of a microorganism, the Agency concludes that risks are unreasonable, it could prevent the activity altogether. However, if the Agency has some risk concerns following review at this stage, it can reduce risks by placing

conditions on the activity or by requiring additional testing. For example, EPA may require the company to monitor the fate of the microorganism, so as to ensure that no unanticipated consequences occur. The Agency could also require engineering or procedural controls to limit incidental releases of the microorganism. The Agency also may impose restrictions such as limiting production or import volumes or confining a field test to a certain area.

4. Risk Reduction due to Action Taken in Response to Regulatory Oversight

The risk reduction potential of the rule as discussed above may be realized through a number of different actions taken during the review process by both EPA and the regulated community.

For example, some important risk reduction may begin during laboratory research, as some researchers could be encouraged to design microorganisms that are less likely to exhibit novel behaviors of concern in an attempt to reduce the level of review and thereby avoid costs. Researchers may be encouraged to develop microorganisms that do not exhibit novel patterns of survival or dissemination in the environment.

Similarly, changes that reduce risk may occur during Agency review. With regard to an environmental application of a new microorganism, a researcher could revise a planned field test to accommodate Agency risk concerns. For fermentation-system activities, risk reduction also may begin prior to or during formal EPA review if companies revise procedures to allow for higher levels of containment or control in response to Agency concerns. Companies also may develop the information that will reduce uncertainty about a microorganisms' behavior and include the information in their submission. These actions directly serve to reduce risk by reducing the probability that a new microorganism exhibiting a phenotypic trait injurious to human health or the environment will become established outside of its controlled site.

C. Qualitative Assessment of Incremental Benefits

The incremental benefits associated with the requirements contained in the rule arise in connection with the risk reduction potential of the rule (with risk reduction achieved as detailed above). By reducing risk, social costs associated with remediation of damages to health and the environment can be avoided. The rule also contributes to greater regulatory efficiency, as it is estimated that the rule will provide the public with more risk reduction per dollar expended. Finally, the pace of commercialization of certain products could be enhanced.

The remainder of this section will present the rationale behind EPA's qualitative incremental benefits assessment and provide further insight into the characterization of the benefits of the rule's requirements.

1. Sources of Incremental Benefits

In its oversight of microorganisms under TSCA, EPA intends to focus on those microorganisms that are most likely to pose the greatest uncertainty regarding risk to human health and the environment. To achieve this focus, the Agency will regulate only intergeneric or "new" microorganisms and will use its authority under TSCA section 5(h)(4) to reduce reporting requirements for some microorganisms that are determined to pose no unreasonable risk to human health or the environment.

With regard to reporting exemptions, EPA stated in its Policy Statement as part of the "1986 Coordinated Framework," that certain contained uses of microorganisms may also warrant a TSCA section 5(h)(4) exemption. This rule will exempt certain microorganisms that are used in a manner minimizing their release to the environment from full reporting requirements. Moreover, the rule describes an exemption for two species of Rhizobia and Bradyrhizobia when tested in the environment under certain conditions.

Thus, as a result of these exemptions from reporting under section 5(h)(4) of TSCA for certain microorganisms and uses which present less uncertainty, reporting burden for such products under the rule will be reduced compared to current policy. Further, since reporting requirements for the balance of potentially regulated products under the rule would be no more burdensome than under current oversight policies, it is clear that the rule will increase the efficiency of EPA's regulatory program under TSCA.

In addition to enhanced regulatory efficiency, the rule would also make reporting in connection with R&D conducted outside of a contained structure mandatory. The effect of this change in policy (such reporting is now voluntary) should enhance EPA's regulatory program by allowing proposals for field trials to be reviewed by the Agency prior to receiving trial data at the general commercial use stage of a microorganism, thus allowing any potential untoward effects of the microorganism to be identified sooner (i.e., before a field trial). Since the Agency strongly encourages and has received voluntary submissions in connection with field trials under the current policy, this policy change is not expected to be associated with significant impacts; however, to the extent that voluntary submissions have not been submitted, the change would provide for an increase in social benefits.

2. Characterization of Benefits

The incremental risk reduction benefits expected to accrue in association with the requirements of the rule are principally due to the avoidance of potential costs of damage to health and the environment. To the extent that adverse effects are irreversible or only partially reversible, resulting costs may be quite large. Thus, although the magnitude of potential costs were not quantifiable, EPA judges the ability of the rule to minimize the probability of such a burden on society to be of substantial value.

Further, to the extent that these costs are transferred from society at large back to the biotechnology sector through compliance with EPA oversight mechanisms, equity is enhanced.

Also, issuance of EPA's rule is likely to avoid a patchwork of state and local regulations that have begun to develop in the absence of a comprehensive federal rule; thus, businesses will have a level playing field and may find it much easier to comply. Inconsistent and uneven regulations across regions could raise rule familiarization costs and reporting costs dramatically, and distort choices of locations for research and production. They also could narrow the potential market for biotechnology products, thereby dampening profit expectations and innovative activities. If a uniform federal rule is put in place, the industry may avoid many of these problems.*

The industry also should benefit from the rule through the "seal of approval" that the public may perceive to be attached to microorganisms reviewed by the Agency. This benefit is already available for many products under the current policy framework. This would be a benefit to society as a whole to the extent that it increases public confidence and removes public opposition to the development of safe and useful products, thus creating a more favorable environment for biotechnology innovators. (This benefit would result from any federal rule that allayed public concerns and is not necessarily a unique benefit of one particular option.)

One type of evidence that this benefit is real lies in the fact that manufacturers are now willing to make voluntary PMN submissions in connection with R&D. This may indicate that they feel that the public relations benefits

* If the federal rule is viewed as an alternative to a collection of state and local regulations, the federal rule's costs and risk-reduction benefits would be measured incrementally to the costs and benefits of state and local regulations.

of the submissions outweigh their costs, though it could also be that voluntary submissions are made for liability reasons or to help prevent regulatory delays in the future.

The rule could also benefit the industry by reducing uncertainty about future regulations. Uncertainty has been mentioned as an industry concern in several sources, including the ICF 1988 survey of the biotechnology industry (ICF 1988) and the 1991 survey update (see Appendix B), a study by Ann Vidaver (Biotechnology 1990), and "Biotechnology: Delays in and Status of EPA's Efforts to Issue a TSCA Regulation" (GAO 1992).

The General Accounting Office (GAO) interviewed officials from three biotechnology associations - The Association of Biotechnology Companies (ABC), The Industrial Biotechnology Association (IBA) (which together now constitute the Biotechnology Industry Association (BIO)), and The Applied BioTreatment Association (ABTA). Representatives from these associations indicated to GAO that the lack of a final TSCA biotechnology regulation has caused uncertainty and is hindering the industry's ability to conduct long-term planning and raise capital for new product research because researchers and investors normally consider the costs of meeting regulatory criteria in investment decisions. The GAO report also cited an official from the Office of Technology Assessment (OTA) who testified that "the failure to promulgate final regulations has led to complaints by industry representatives that the regulatory approval process is unclear and inhibits investment" (GAO 1992).

In addition, an EPA researcher in the area of bioremediation suggested that benefits from increased certainty depend strongly on whether regulations are very specific as to what is permitted, or if the regulators (including those charged with implementing statutes other than TSCA) proceed on a case-

by-case basis. The former approach may reduce delays in product development, but the latter would not significantly reduce uncertainty (Shields 1990).

Finally, unless there is coordination among federal, state, and local agencies regarding notification and other regulatory requirements, uncertainty will remain. For example, there could be duplication and overlapping of regulations without a coordinated framework. As a result, companies may be unable to decide to which agency to submit information for review. This uncertainty may lead to additional costs and delays in the development of commercial products.